REMARKS/ARGUMENTS

Claim 28 has been amended to incorporate the limitations of claim 31. Claim 31 has been canceled. Claim 32 is amended to change its dependency from claim 31 to claim 28. No new matter is added. Upon entry of the above amendments, claims 28-30 and 32-40 are pending. Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

Claims 28-40 are rejected under 35 U.S.C. 103(a) as obvious over the combination of Hochlowski et al., Tiacumicins, a novel complex of 18-membered macrolides. II. Isolation and structure determination. J. Antibiotics: 575-588,1987, McAlpine et al. (U.S. Patent No. 4,918,174), Coronelli et al. (U.S. Patent 3,978,211), Waters et al. (U.S. Patent 4,632,902) Hoefle et al. (U.S. Patent 7,067,544) and Demain et al., Manual of Industrial Microbiology and Biotechnology, American Society of Microbiology, Washington, D.C. 1989, pp 123-126. Applicants respectfully traverse.

None of Hochlowski, McAlpine, Coronelli, and Waters discloses the use of a resin during the culturing of the microorganism. Further, Coronelli does not disclose the production of tiacumicins but rather lipiarmycin.

Only Hoefle and Water discuss the use of a resin. In Hoefle, the resin XAD-16 is used during fermentation so that epothilones that are produced by fermentation are absorbed. Epothilones as described in Hoefle are very different in chemical structure to tiacumicins, and there is no teaching in Hoefle or any of the other cited references that tiacumicins can be similarly absorbed by a resin during fermentation. Water teaches the use of a resin to absorb antibiotics from a body fluid specimen without removal of the infecting bacteria contained in the specimen. Such absorption occurs in an environment that is different from that encountered during fermentation. Accordingly, there is no reasonable basis or apparent reason to combine Water or Hoefle with other cited references to arrive at the presently claimed process. Applicants have previously submitted these remarks, but the Examiner does not comment on the merit of these remarks in the present Office Action.

Moreover, the presently claimed process exhibits unexpected results. Applicants have found that the use of an absorbent resin in the nutrient medium during the culturing of the microorganism unexpectedly

resulted in a change in the profile of the fermentation product by increasing the production of tiacumicin B and suppressing the other related tiacumicins.

The Examiner comments at pages 3-4 of the Office Action that "it is unclear that the profile of fermentation product necessarily results in greater production of Tiacumicin B as alleged using any strain or any adsorbent resin. It is apparent that specific conditions and a specific strain are required to achieve the touted results."

In response, Applicants have now amended claim 1 to limit the absorbent to "absorbent resin" and submitted a declaration and Exhibit 1 under Rule 132. As shown at Fig. 1, Exhibit 1, using resin according to the process described in the claims of the '863 application significantly changes the profile of the fermentation product. As shown in Fig. 1, the use of Medium No. 66 for fermentation, which contains no resin, shows a production profile of almost a 1:1 ratio of tiacumicin B and tiacumicin C. In fact, all but Medium No. 74, which contains resin XAD-16, show product profiles with excess amount of tiacumicin C. When the XAD-16 resin is added as indicated in Medium No. 74, the product profile contains a very small amount of tiacumicin C with mostly tiacumicin B being present. As explained by the declarant, this result would have been unexpected for an artisan in the field. Similarly, as shown in Figs. 2-3, Exhibit 1, the unexpected benefit shown in Fig. 1 in connection with XAD-16 resin can be similarly obtained from the use of other resins, including XAD-7, XAD-16HP, HP-20, XAD-1180, and XAD-2 in various amounts. Based on Figs. 1-3, the declarant concludes that it is his belief that the unexpected benefit shown in Figs. 1-3 using various absorbent resins in various amounts can reasonably be extrapolated to an absorbent resin in general.

For reasons expressed above, claims 28-30 and 32-40 are patentable under 35 U.S.C. 103(a) over the combination of Hochlowski et al.,McAlpine et al., Coronelli et al., Waters et al., Hoefle et al., and Demain et al. Applicants respectfully request that the Examiner withdraw the rejections of the claims under the rejection of claims 35 U.S.C. 103(a).

It is believed that no fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN PONTANI LIEBERMAN & PAVANE LLP

By _____

Kent H. Cheng
Reg. No. 33,849
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

Dated: August 7, 2008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Youe-Kong Shue et al. Serial No.: 10/520,863 Filed: July 13, 2005 For: Tiacumicin Production	Examiner: Irene Marx Group Art: 1651

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.132

I, Youe-Kong Shue, citizen of USA, residing at 7869 Via Teca, Carlsbad, CA 92009, hereby declare that:

1. I received the Ph.D.(degree) degree in Organic Chemistry (major) from University of Pittsburgh in Pittsburgh, PA, USA in 1982.
2. I have been Vice President, Clinical Development of Optimer Pharmaceuticals, Inc., in San Diego, CA since 2006. My experience includes new drug research and development in Neuroscience area and Infectious Disease areas.
3. I am one of the co-inventors of U.S. Patent Application No. 10/520,863 ("the '863 application") entitled " Tiacumicin Production ."

4. I have carefully reviewed the specification and claims of the '863 application and the Office Action dated May 13, 2008 in connection with the '863 application. For the reasons expressly set forth below, it is my belief that the use of an absorbent resin (in general) in a nutrient medium for fermentation based on the claims of the '863 application resulted in significant and unexpected benefits.
5. The tests described in Exhibit 1 were conducted and/or directed by me.
6. As shown at Fig. 1, Exhibit 1, using resin according to the process described in the claims of the '863 application significantly changes the profile of the fermentation product. As shown in Fig. 1, the use of Medium No. 66 for fermentation, which contains no resin, shows a production profile of almost a 1:1 ratio of tiacumicin B and tiacumicin C. In fact, all but Medium No. 74, which contains resin XAD-16, show product profiles with excess amount of tiacumicin C. When the XAD-16 resin is added as indicated in Medium No. 74, the product profile contains a very small amount of tiacumicin C with mostly tiacumicin B being present.
7. As shown in Fig. 2, Exhibit 2, the benefit shown in Fig. 1 in connection with XAD-16 resin can be similarly obtained from the use of other resins, including XAD-7, XAD-16HP, HP-20, XAD-1180, and XAD-2. The yield of tiacumicin B using these resins can reach about or above 200 mg/L.
8. As shown in Fig. 3, the significant increase of the yield of tiacumicin B can be obtained from use of various amount of resin. Although the yield of ticumicin B using certain amount of resin (for example 2% (w/w) and 3% (w/w)) is

higher than the yield using other amount of reins (for example 1% (w/w)), the yield of tiacumicin B using all these different amounts of resin is all significantly improved. A yield of more than 100 mg/L of tiacumicin B is obtained by using only 1% (w/w)of XAD-16 resin.

9. Therefore, it is my belief that the unexpected benefit shown in Figs. 1-3 using various absorbent resins in various amounts can reasonably be extrapolated to an absorbent resin in general.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: August 07, 2008 By: _____ (signature)

Youe-Kong Shue (Printed name)

Exhibit 1: The Progress Report of OPT-40 Project

Fermentation using different type of resin in a nutrition medium

The following fermentation mediums were respectively used of making tiacumicin B to examine the effect of various resins on the yield of tiacumin B.

Control medium: 1% Fish powder, 2% Glucose, 0.05%K2HPO4, 0.05%MgSO4.7H2O, 0.03%KCl, and 0.3%CaCO3, based on the total weight of the medium.

Medium No. 63: Control medium +1% Fish powder+2% Glucose, based on the total weight of the medium.

Medium No. 64: Control medium +1.5% Fish powder+3% Glucose, based on the total weight of the medium.

Medium No. 65: Control medium+ 2% Fish powder+4% Glucose, based on the total weight of the medium.

Medium 66: Control medium.

Medium No. 67: Control medium+ 1% Fish powder+1% Starch, based on the total weight of the medium.

Medium No. 68: Control medium +1% Fish powder+2% Starch, based on the total weight of the medium.

Medium No. 69: Control medium+ 1% Fish powder+3% Starch, based on the total weight of the medium.

Medium No. 70: Control medium+ 0.2% yeast extract, based on the total weight of the medium.

Medium No. 71: Control medium+0.1% methionine, based on the total weight of the medium.

Medium No. 72: Control medium+ 0.2%casamino acids, based on the total weight of the medium.

Medium No. 73: Control medium+ 0.1%cysteine, based on the total weight of the medium.

Medium No. 74: Control medium+ 2%XAD-16, based on the total weight of the medium.

Medium No. 75: Control medium+ 0.1% glycine, based on the total weight of the medium.

Medium No. 76. Control medium+ 0.2% peptone, based on the total weight of the medium.

Medium No.: 136: Control medium + 0.25% casamino acid + 0.25% yeast extract+2% XAD-7, based on the total weight of the final medium.

Medium No. 137: Control + 0.25% casamino acid + 0.25% yeast extract+2% HP-20, based on the total weight of the final medium.

Medium No. 138: Control + 0.25% casamino acid + 0.25% yeast extract+2% XAD-2, based on the total weight of the final medium.

Medium No. 139: Control + 0.25% casamino acid + 0.25% yeast extract+2%XAD-16HP.

Medium No. 140: Control + 0.25% casamino acid + 0.25% yeast extract+2% XAD-1180.

Medium No. 141: Control + 0.25% casamino acid + 0.25% yeast extract+2% XAD-16.

Medium No. 143: Control + 0.25% casamino acid + 0.25% yeast extract+1% XAD-16.

Medium No. 144: Control + 0.25% casamino acid + 0.25% yeast extract+3% XAD-16.

Medium No. 145: Control + 0.25% casamino acid + 0.25% yeast extract+4% XAD-16.

The fermentation tests were carried out according to the following protocol:

1. Take stored mycelium solution 1 ml, put into seed medium 50 ml / 250 ml flask (S1); then incubate S1 for 3 days in shaker box at 220 rpm , 30^0C .

2. Transfer S1 above into seed medium 125 ml / 500 ml flask (S2);then incubate S2 for 3 days in shaker box at 220 rpm , 30^0C .

3. Transfer S2 above into batch medium 2500 ml / 5L fermentor .

4. Set operation conditions : agitation at 300 rpm , aeration 0.7 vvm and temperature at 32^0C .

5. Maintaining dissolved oxygen (D.O.) at > 20 % by adjusting agitation and aeration .

6. After 24 hours cultivation, start to analyze the residual glucose and OPT-40 twice a day; when the residual glucose is 0 g/L, begin to feed feeding medium into the fermentator.

7. Keep the residual glucose below 2.0 g/L throughout the OPT-80 production phase.

8. When the foaming is observed, add some antifoam (Sigma A6426) to control the foaming level .

9 When all feeding medium is fed, harvest and collect the broth in glass bottle, store them in 4^0C refrigerator for downstream recovery .

The final yield of tiacumcin B using the above Medium Nos. 63-76, among which only Medium No. 74 contains resin, is shown in Fig. 1 below.

The final yield of tiacumcin B using the above Medium Nos. 136-141, which respectively comprise different type of resin, is shown in Fig. 2 below.

The final yield of tiacumicin B using the above Medium Nos. 141-145, which respectively comprise different concentration of resin, is shown in Fig. 3 below.

Note that OPT-40 mentioned above and referred to in Figs. 1-3 below is tiacumicin B. OP-40 (bead) means OPT-40 absorbed on resin. The final yield of tiacumicin B using the Medium Nos. 63-76, among which only Medium No. 74 contains resin, is shown in Fig. 1. The presence of resin clearly increased the formation of OPT-40.